REMARKS

In the Office Action dated November 2, 2005, the Examiner rejected pending claims 48-53 and 55-60 under 35 U.S.C. § 112, first paragraph, as allegedly containing new subject matter not present in the specification as originally filed. Further, the Examiner rejected claims 48-53, 55, and 57-60 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Further, the Examiner rejected claims 48-53 and 55-60 under 35 U.S.C. § 102(b), as allegedly being anticipated by the Plested et al reference (Infect Immun. 1999 Oct; 67(10): 5417-26). The Examiner refused to grant priority to the subject claims from U.S. Provisional Applications 60/196,305, filed 4/12/00, and 60/156,940, filed 09/30/99, alleging that the subject claims lack descriptive support in Provisional Applications 60/196,305 and 60/156,940. Thus, Plested, although published after U.S. Provisional Application 60/156,940, was used as a prior art reference under 35 U.S.C. § 102(b).

In a Response dated March 1, 2006 to the pending Office Action, Applicants filed an amended set of claims and an explanation of why the pending set of claims is allowable. Applicants' arguments included an explanation of how the full range of embodiments covered by the pending claims was enabled by the specification of the subject application.

In an Advisory Action dated March 14, 2006, the Examiner maintained the 35 U.S.C. § 112, first paragraph rejection of remaining claims 48, 49, 55, and 56 on the grounds that the rejection was a new matter rejection, not an enablement rejection. The Examiner further alleged that the 35 U.S.C. § 112, first paragraph issue with the pending claims is not the antigenicity or epitope reactivity of all *Neisseria* strains containing the conserved epitope (or of *N. meningitidis* immunotypes L1, L3, L7, L8, L9, L10, L11, and L12) with monoclonal antibody B5. Rather, the Examiner alleged that the subject application lacks descriptive support for the claimed method, as described in detailed in the Claims Rejections section hereinbelow.

The Examiner further maintained the rejection of claims 48, 49, 55, and 56 under 35 U.S.C. § 102(b) in view of Plested. As a result of the new matter issues described above, the Examiner refused to grant priority to the subject claims to U.S. Provisional Applications 60/196,305 and 60/156,940. Thus, Plested was maintained as an allegedly anticipatory reference under 35 U.S.C. § 102(b).

The Examiner admitted, however, that the other grounds for rejection cited in the Final Office Action dated November 2, 2005 did not apply to the amended set of claims filed on March 1, 2006. Thus, the only remaining issues with the pending set of claims filed on March 1, 2006 were (a) the new matter rejection of claims 48, 49, 55, and 56 under 35 U.S.C. § 112, first paragraph and (b) the 35 U.S.C. § 102(b) rejection in view of Plested.

In a Response dated April 24, 2006 to the pending Office Action, Applicants traversed the new matter rejection, by showing that the subject matter of the pending claims was fully described in the specification as filed.

In an Advisory Action dated May 5, 2006, the Examiner stated:

> "Although the amendments to claims 48 and 55 and Applicants' arguments appear to potentially overcome the pending new matter rejection, and therefore the art rejection of record, the new amendments change the scope of the claims and require new ground(s) of rejection at least under 35 U.S.C. § 102 and/or 103."

Thus, the only grounds of rejection potentially remaining were prior art rejections in view of yet-to-be cited documents.

In a telephone interview, with Applicants' Representative, Marc Tritel, on August 29, 2006, Applicants' Representative pointed out to the Examiner that, with respect to the set of claims filed February 22, 2005, all prior art rejections raised in the May 16, 2005 Office Action had been overcome. Since the current set of claims at that time was narrower than the set of claims filed February 22, 2005, and since Applicants expected the Examiner to have cited the most relevant prior art in the May 16, 2005 Office Action, Applicants considered the current set of claims at the time to be in condition for allowance, without requiring from the Examiner additional searching and/or assessment of patentability in view of the prior art. The Examiner replied that not all of the most relevant prior art documents were cited in the May 16, 2005 Office Action; for example, Pavliak et al. had not been cited. Pavliak is cited in the Information Disclosure Statement accompanying this Amendment, to ensure the Examiner's consideration.

The present Response is intended to be fully responsive to all issues raised by the Examiner in prior Office Actions and in the telephone interview. The amended set of claims file herewith are fully described in the subject specification, as explained hereinbelow, and thus are in condition for allowance. Favorable reconsideration and allowance of the application is respectfully requested.

Status of Claims

Claims 48, 49, 55, and 56 are pending in the application. Claims 48, 49, 55, and 56 have been rejected. Claims 48 and 55 have been amended. Claims 62-81 have been added.

The Telephone Interview

Initially, Applicants wish to thank the Examiner, Examiner Devi, for granting and attending the telephone interview, with Applicants' Representative, Marc Tritel, on August 29, 2006. As described hereinabove, patentability of the claims in view of the prior art was discussed.

CLAIM REJECTIONS

35 U.S.C. § 112, First Paragraph Rejections

In the November 2, 2005 Office Action, the Examiner rejected claims 48-53 and 55-60 under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter not contained in the specification as filed. The Examiner alleged that the subject application lacks descriptive support for the administration of any "immunogenic composition comprising an inner core of a *Neisseria* LPS, wherein a PEtN moiety is linked to position 3 of a HepII moiety of the inner core," wherein the composition, upon administration to a host, elicits an antibody that recognizes all *N. meningitidis* immunotypes L1, L3, L7, L8, L9, L10, L11, and L12. Further, the Examiner alleged that the only immunogenic composition disclosed in the subject specification is a *galE* mutant of *N. meningitidis*. Thus, the Examiner alleged that the subject specification does not provide descriptive support for the claimed method of use, utilizing any immunogenic composition comprising an inner core of a *Neisseria* LPS, wherein a PEtN moiety is linked to position 3 of a HepII moiety of the inner core.

Applicants respectfully disagree. Amended claims 48-49 and 55-56 and new claims 62-69 are directed to methods for (1) eliciting in a host an antibody that recognizes [claims 48-49 and 62-65] or (2) immunizing a host against [claims 55-56 and 66-69] *Neisseria meningitidis* (NM) immunotypes L1, L3, L7, L8, L9, L10, L11, and L12, comprising administering an immunogenic composition, comprising an inner core of a *Neisseria* lipopolysaccharide (LPS), wherein a PEtN moiety is linked to position 3 of the HepII moiety thereof, wherein the antibody binds to an inner core LPS of NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12; and is capable of conferring passive protection against NM immunotype L3. New claims 70-81 are directed to methods for (3) eliciting in a host an antibody that recognizes [claims 70-75] or (4) immunizing a host against [claims 76-81] a majority of naturally occurring strains of NM, comprising administering an immunogenic composition, comprising an inner core of a LPS, wherein a PEtN moiety is linked to position 3 of the HepII moiety thereof, wherein the antibody binds to an inner core LPS of a majority of naturally occurring strains of NM; and is capable of conferring passive protection against a galE mutant of an L3 immunotype *Neisseria meningitidis* strain. Each limitation in amended claims 48-49 and 55-56 and new claims 62-81 was fully described in the subject specification as filed, as described hereinbelow.

Limitation #1: "A method for eliciting in a host an antibody that recognizes NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12, comprising administering an immunogenic composition, comprising an inner core of a *Neisseria* LPS, wherein a PEtN moiety is linked to position 3 of the HepII moiety thereof" (claims 48-49 and 62-65).

The subject specification as filed clearly described a vaccine comprising a ***conserved epitope***, wherein the epitope is defined by the presence of PEtN at the 3-position of Hep2 of the inner core. Contrary to the Examiner's allegations in the November 2, 2005 Office Action, the *galE* NM mutant was utilized in the subject specification ***not*** as a principal embodiment of the vaccines of the subject invention, but rather as a ***means*** to elicit monoclonal antibody B5, which in turn was used as a means to define the conserved epitope central to vaccines of the present invention:

> "The ***epitope against which B5 reacts*** has been characterized and ***can be used to form the basis of a vaccine*** to prevent *Neisseria* infections" (page 6, third full paragraph; emphasis added).

Thus, contrary to the Examiner's allegations, the vaccines of present invention are defined by the presence of the conserved epitope, not by the *galE* mutation.

Further, the subject specification clearly describes the conserved epitope as being characterized by the presence of PEtN at the 3-position of Hep2 of the inner core:

> "The immunogenic component of the present invention is typically only limited by the requirement for a PEtN moiety linked to the 3-position of HepII of the inner core" (page 9, fifth paragraph).

Further, the claims of the subject specification as filed describe a vaccine comprising a conserved epitope, defined by the presence of PEtN at the 3-position of Hep2 of the inner core, and its use in eliciting antibodies against pathogenic *Neisseria* strains:

> "1. A vaccine for the treatment of disease caused by pathogenic *Neisseria*, the vaccine comprising an immunogenic component based on the inner core of a *Neisseria* lipopolysaccharide, LPS, and being capable of eliciting functional antibodies against a majority of the strains within the species of the pathogenic *Neisseria*.
>
> 10. A vaccine according to claim 1, **wherein the immunogenic component is an epitope on the LPS inner core characterized by the presence of a phosphoethanolamine moiety linked to the 3-position at HepII of the inner core**, or is a functional equivalent thereof" (emphasis added).

Thus, the subject specification as filed described administration of a vaccine comprising a conserved epitope, defined by the presence of PEtN at the 3-position of Hep2 of the inner core, for elicitation of antibodies that recognize *Neisseria*.

Further, the subject specification clearly describes the *Neisseria* strains that are recognized by antibodies elicited by vaccines of the present invention:

> "An inner core structure recognized by MAb B5 is conserved and accessible in 26/34 (76%) of Group B and 78/112 (70%) of Groups A, C, W, X, Y, and Z strains. *Neisseria meningitidis* strains which possess this epitope are immunotypes in which PEtN is linked to the 3-position of the β-chain HepII of the inner core" (page 21, first paragraph).

> "Of the 12 immunotypes, MAb B5 recognized the LPS of strains in which the inner core oligosaccharide has a PEtN linked to the 3-position of HepII (Table 2 and Figure 1). Thus, immunotypes L2, L4, L6 did not react with MAb B5, **whereas immunotypes L1, L3, L7-12 were recognized by MAb B5**" (page 31, second full paragraph; emphasis added).

Accordingly, the subject specification as filed described Limitation #1; namely, a method of eliciting an antibody that recognizes all *N. meningitidis* immunotypes L1, L3, L7, L8, L9, L10, L11, and L12, comprising administration of any vaccine comprising the conserved epitope, wherein the conserved epitope is defined by the presence of PEtN at the 3-position of Hep2 of the inner core.

Limitation #2: wherein the antibody binds to an inner core LPS of NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12 (claims 48, 55, 70, and 76).

As described hereinabove in the discussion of Limitation #1, the subject specification as filed described a conserved epitope, defined by the presence of PEtN at the 3-position of Hep2 of a *Neisseria* inner core LPS, and described that vaccines containing the conserved epitope elicit antibodies that recognize NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12. "Recognize" and "bind" are recognized in the art to by synonyms in the context of antibody recognition, and are utilized synonymously in the subject specification, as shown by the quotation below:

> "We have shown that MAb B5 can bind to the core LPS of wild-type encapsulated MC58 (B.15.P1.7,16 immunotype L3) organisms *in vitro* and *ex vivo*. An inner core structure recognized by MAb B5 is conserved and accessible in 26 of 34 (76%) of group B and 78 of 112 (70%) of groups A, C, W, X, Y, and Z strains" (page 21, first paragraph; emphasis added).

Further, the subject specification as filed described that the binding site of the elicited antibodies to the bacteria is inner core LPS:

> "The antibodies generated by the vaccine of this invention bind to inner core elements of the pathogenic target bacterium" (page 13, second full paragraph).

Accordingly, the subject specification as filed described Limitation #2; namely, wherein the antibody binds to an inner core LPS of NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12.

Limitation #3: wherein the antibody...is capable of conferring passive protection against a galE mutant of an L3 immunotype Neisseria meningitidis strain (claims 48, 55, 70, and 76).

The subject specification described elicitation of antibodies that confer passive protection against MAb B5-reactive strains, including a galE mutant of MC58, an L3 immunotype LM strain:

> "The immunogenic elements of the invention are preferably those shown to elicit antibodies having opsonic and bactericidal activity, and shown to generate antibodies which confer passive protection in in vivo models" (page 12, third full paragraph).

> "Using the 5-day-old infant rat model we have demonstrated that two doses MAb B5 are able to reduce bacteremia against challenge with 1 x 10^8 cfu/ml Neisseria meningitidis MC58 galE mutant i.p. compared to no antibody controls" (page 57, last paragraph).

Accordingly, the subject specification as filed described Limitation #3; namely, wherein the antibody is capable of conferring passive protection against a galE mutant of an L3 immunotype *Neisseria meningitidis* strain.

Limitation #4: A method for immunizing a host against NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12, comprising administering an immunogenic composition, comprising an inner core of a *Neisseria* LPS, wherein a PEtN moiety is linked to position 3 of the HepII moiety thereof" (claims 55-56 and 66-69).

The subject specification as filed described that immunogenic compositions of the present invention contain a conserved epitope useful in vaccination against *Neisseria*:

> "In a first aspect, the invention relates to a vaccine for the treatment of disease caused by *Neisseria* infection, the vaccine comprising an immunogenic component of *Neisseria* strains. The vaccine presents a conserved and accessible epitope that in turn promotes a functional and protective response" (page 5, fourth paragraph; emphasis added).

> "The epitope against which B5 reacts has been characterized and can be used to form the basis of a vaccine to prevent *Neisseria* infections" (page 6, third full paragraph; emphasis added).

Further, the subject specification clearly describes the conserved epitope as being characterized by the presence of PEtN at the 3-position of Hep2 of the inner core:

> "The immunogenic component of the present invention is typically only limited by the requirement for a PEtN moiety linked to the 3-position of HepII of the inner core" (page 9, fifth paragraph).

Further, the claims of the subject specification as filed describe a vaccine comprising a conserved epitope, wherein the epitope is defined by the presence of PEtN at the 3-position of Hep2 of the inner core, and its use in immunization against *Neisseria* infection:

"1. A vaccine for the treatment of disease caused by pathogenic *Neisseria*, the vaccine comprising an immunogenic component based on the inner core of a *Neisseria* lipopolysaccharide, LPS, and being capable of eliciting functional antibodies against a majority of the strains within the species of the pathogenic *Neisseria*.

10. A vaccine according to claim 1, **wherein the immunogenic component is an epitope on the LPS inner core characterized by the presence of a phosphoethanolamine moiety linked to the 3-position at HepII of the inner core**, or is a functional equivalent thereof" (emphasis added).

Further, the specificity of the above-described vaccines is described in the subject specification as filed:

"An inner core structure recognized by MAb B5 is conserved and accessible in 26/34 (76%) of Group B and 78/112 (70%) of Groups A, C, W, X, Y, and Z strains. *Neisseria meningitidis* strains which possess this epitope are immunotypes in which PEtN is linked to the 3-position of the β-chain HepII of the inner core" (page 21, first paragraph).

"Of the 12 immunotypes, MAb B5 recognized the LPS of strains in which the inner core oligosaccharide has a PEtN linked to the 3-position of HepII (Table 2 and Figure 1). Thus, immunotypes L2, L4, L6 did not react with MAb B5, **whereas immunotypes L1, L3, L7-12 were recognized by MAb B5**" (page 31, second full paragraph; emphasis added).

Thus, the subject specification clearly described and showed that antibodies elicited by the conserved epitope, or an immunogenic composition comprising same, recognize NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12. Accordingly, the subject specification described that vaccines comprising a conserved epitope, defined by the presence of PEtN at the 3-position of Hep2 of the inner core, are useful in immunization against NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12.

Accordingly, the subject specification as filed described Limitation #4; namely, a method of immunizing a host against NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12, comprising administering an immunogenic composition, comprising an inner core of a *Neisseria* LPS, wherein a PEtN moiety is linked to position 3 of the HepII moiety thereof.

Limitation #5: A method of eliciting in a host an antibody that recognizes a majority of naturally occurring strains of NM, comprising administering an immunogenic composition, comprising an inner core of a LPS, wherein a PEtN moiety is linked to position 3 of the HepII moiety thereof (claims 70-75).

As described hereinabove (discussion of Limitation #4), the subject specification as filed described immunogenic compositions that contain a conserved epitope useful in vaccination against *Neisseria*, wherein the conserved epitope is characterized by the presence of PEtN at the 3-position of Hep2 of the inner core.

Further, the subject specification as filed describes that immunogenic compositions containing the conserved epitope of the present invention elicit antibodies that recognize the majority of naturally occurring strains of NM:

> "In summary, we report that a monoclonal antibody, designated B5, has identified a cross-reacting epitope on the LPS of the majority of naturally occurring, but genetically diverse strains of *Neisseria meningitidis*" (paragraph beginning on page 21; emphasis added).

Thus, the subject specification as filed described that the conserved epitope of the present invention is present on the majority of naturally occurring strains of NM, and is recognized by antibodies elicited by vaccines comprising the conserved epitope of the present invention.

Accordingly, the subject specification as filed described Limitation #5; namely, a method of eliciting in a host an antibody that recognizes a majority of naturally occurring

strains of NM, comprising administering an immunogenic composition, comprising an inner core of a LPS, wherein a PEtN moiety is linked to position 3 of the HepII moiety thereof.

Limitation #6: A method of immunizing a host against a majority of naturally occurring strains of NM, comprising administering an immunogenic composition, comprising an inner core of a LPS, wherein a PEtN moiety is linked to position 3 of the HepII moiety thereof (claims 76-81).

As described hereinabove (discussion of Limitation #4), the subject specification as filed described immunogenic compositions that contain a conserved epitope useful in vaccination against *Neisseria*, wherein the conserved epitope is characterized by the presence of PEtN at the 3-position of Hep2 of the inner core.

Further, as described hereinabove, (discussion of Limitation #5), the subject specification as filed describes that immunogenic compositions containing the conserved epitope of the present invention elicit antibodies that recognize the majority of naturally occurring strains of NM.

Accordingly, the subject specification described that vaccines comprising a conserved epitope, defined by the presence of PEtN at the 3-position of Hep2 of the inner core, are useful in immunization against the majority of naturally occurring strains of NM.

Accordingly, the subject specification as filed described Limitation #6; namely, a method of immunizing a host against a majority of naturally occurring strains of NM, comprising administering an immunogenic composition, comprising an inner core of a LPS, wherein a PEtN moiety is linked to position 3 of the HepII moiety thereof.

Limitation #7: wherein said inner core LPS... is accessible to said antibody in a presence of an outer core LPS (claims 62, 66, 72, and 78).

The subject specification as filed described conserved epitopes of the present invention that are recognized in the presence of an outer core LPS:

> "The immunogenic component is suitably one which elicits an immune response in the presence and in the absence of outer core LPS" (paragraph beginning on page 7).

Accordingly, the subject specification as filed described Limitation #7; namely, wherein said inner core LPS is accessible to said antibody in a presence of an outer core LPS.

Limitation #8: wherein said inner core LPS...is accessible to said antibody in a presence of a bacterial capsule (claims 63, 67, 73, and 79).

The subject specification as filed described conserved epitopes of the present invention that are recognized in the presence of a bacterial capsule:

> "Preferably the immunogenic element of the vaccine is accessible in the presence of bacterial capsule" (page 12, last full paragraph).

Accordingly, the subject specification as filed described Limitation #8; namely, wherein said inner core LPS is accessible to said antibody in a presence of a bacterial capsule.

Limitation #9: wherein said immunogenic composition comprises said inner core of a *Neisseria* LPS conjugated to a protein or peptide (claims 64, 68, 74, and 80).

The subject specification as filed described immunogenic compositions comprising an inner core of a *Neisseria* LPS conjugated to a protein or peptide:

> "Vaccines of the present invention are preferably formulated vaccines in which any of the immunogenic components of the vaccine may be conjugated, and any suitable agent for conjugation may be used... Examples of agents for

conjugation include proteins from homologous or heterologous species. In this way, the immunogenic component of the present invention forms a saccharide peptide conjugate" (paragraph beginning on page 13; emphasis added).

Accordingly, the subject specification as filed described Limitation #9; namely, wherein said immunogenic composition comprises said inner core of a Neisseria LPS conjugated to a protein or peptide.

Limitation #10: wherein said inner core of a *Neisseria* LPS is an inner core of a *Neisseria meningitidis* LPS (claims 65, 69, 75, and 81).

The subject specification as filed described immunogenic compositions comprising an inner core of a *Neisseria meningitidis* LPS:

"Using a range of novel monoclonal antibodies, epitopes belonging to the inner core of *Neisseria meningitidis* have been identified which have been found to be accessible to the immune system, and which are capable of stimulating the production of function, protective antibodies" (page 5, last paragraph; emphasis added).

Accordingly, the subject specification as filed described Limitation #10; namely, wherein said inner core of a *Neisseria* LPS is an inner core of a *Neisseria meningitidis* LPS.

Thus, the subject matter of the pending claims was clearly described in the subject specification as filed. Applicants therefore respectfully request that the rejection be withdrawn.

Further, the Examiner alleged that support in the subject specification for immunogenic compositions was limited to compositions derived from *N. meningitidis* inner core, to the exclusion of other *Neisseria* species.

Applicants respectfully disagree. The subject specification clearly describes that the immunogenic component can be derived from *Neisseria* species other than NM:

> "The invention also extends to immunogenic components in other Neisseria species which are related to those identified in *N. meningitidis*, either by function, antibody reactivity or structure. The invention is not limited to pathogenic strains of *Neisseria*. The vaccine of this invention can be derived from a commensural strain of *Neisseria*" (paragraph beginning on page 10).

Thus, the subject specification as filed describes that the conserved epitope of the present invention is present in, and thus may be derived from, a number of *Neisseria* species other than NM. Accordingly, the present invention should not be limited to an immunogenic component derived from NM.

Applicants therefore respectfully request that the rejection be withdrawn.

Thus, the pending claims do not contain new matter over the subject specification as filed, and therefore are in compliance with the requirements of 35 U.S.C. § 112. Applicants therefore respectfully request that the rejection be withdrawn.

35 U.S.C. § 102 Rejections

Further, the Examiner maintained the rejection of claims 48, 49, 55, and 56 under 35 U.S.C. § 102(b) in view of Plested. As a result of the new matter issues described above, the Examiner refused to grant priority to the subject claims to U.S. Provisional Applications 60/196,305 and 60/156,940. Thus, Plested was maintained as an allegedly anticipatory reference under 35 U.S.C. § 102(b).

Applicants respectfully disagree. Plested provides no data disclosing or suggesting elicitation of antibodies that confer passive protection against a galE mutant of an L3 immunotype *Neisseria meningitidis* strain, as recited in the amended claims. Thus, Plested neither discloses nor suggests the subject matter of the subject claims.

Further, as described hereinabove, the pending claims of the subject application contain no new matter over the subject specification as filed. Thus, it is improper to use Plested as an anticipatory reference against the subject specification under 35 U.S.C. § 102(b).

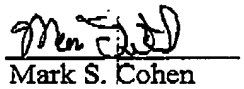
Applicants therefore respectfully request that the rejection be withdrawn.

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 50-3355.

Respectfully submitted,



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